```
L4 ANSWER 1 OF 4 USPATFULL
ACCESSION NUMBER: 2000:80434 USPATFULL
TITLE: Process for encapsulation of caplets in a capsule
                                                                solid dosage forms obtainable by such process Amey, James, Greenwood, SC, United States Cade, Dominique, Colmar, France Maes, Paul, Mortsel, Belgium Scott, Robert, Wasmunster, Belgium Warner-Lamberg Company, Morris Plains
 INVENTOR(S):
 PATENT ASSIGNEE(S):
                                                                              NUMBER
                                                                                                                  DATE
                                                                US 6080426 20000627
US 1996-585549 19960111 (8)
Continuation of Ser. No. US 1994-358137, filed on
 PATENT INFORMATION:
 APPLICATION INFO.:
RELATED APPLN. INFO.:
16
                                                                Dec 1994, now abandoned
Utility
Spear, James M.
Almer, Charles W.
38
 DOCUMENT TYPE
 DOCUMENT TIPE:
PRIMARY EXAMINER:
LEGAL REPRESENTATIVE:
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
                                                                  456
LINE COUNT: 450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for encapsulation of caplets in a capsule comprises the following steps: a. providing empty capsule parts: b. filling at
least
one of said capsule parts with one or more caplets; c. putting said
capsule parts together; and d. treating the combined parts by cold
shrinking. The solid dosage forms obtainable by such aprocess are
tamper-proof in that they cannot be opened in a way to be
reassembled
reassembled
vithout showing such opening process.

IT 34031-32-8, Auranofin
(encapsulation of caplets in capsules in tamper-proof forms)

RN 34031-32-8 USPATFULL
CN Gold, [1-(thio-.kappa.5)-.beta.-D-glucopyranose 2,3,4,6-
tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)
Et 3P - Au + S.
                                                    CH2-OAc
```

L4 ANSWER 2 OF 4 USPATFULL (Continued)
CN Gold, [1-(thio--kappa.S)--beta-D-glucopyranose 2,3,4,6tetraacetato] (triethylphosphine) - (9CI) (CA INDEX NAME)

```
LA ANSWER 2 OF 4 USPATFULL
ACCESSION NUMBER: 1999:155217 USPATFULL
Histanine antagonist, an interleukin-1 antagonist and/or a TMF alpha antagonist in a cosmetic, pharmaceutical or dermatological composition
De Lacharriere, Olivier, Paris, France
Breton, Lionel, Versailles, France
Cohen, Catherine, Paris, France
Breton, Lionel, Versailles, France
Cohen, Catherine, Paris, France
Societe L'Oreal S.A., Paris, France
NUMBER DATE

NUMBER DATE

PATENT INFORMATION: US 1997-879889 19970620 (8)
RELATED APPLIN. INFO:: Division of Ser. No. US 1995-580291, filed on 28
DEC 1995, now patented, Pat. No. US 5658581

NUMBER DATE

PRIORITY INFORMATION: PR 1994-15796 19941228
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Venkar, Jyothsna
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 105
LINE COUNT: 745
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of a histamine antagonist, an interleukin-1-antagonist and/or a TNF antagonist in a cosmetic, pharmaceutical or dermatological composition for treating sensitive skins. It relates especially to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF alpha antagonist for preventing and/or combating skin irritations and/or sores and/or erythema and/or combating skin irritations and/or sores and/or erythema and/or a TNF alpha antagonist for composition containing a histamine antagonist, an interleukin-1 antagonist and/or sensations of inflammation and/or prickling and/or tingling and/or discomfort and/or tightness of the skin and/or mucosae. It also relates to a composition containing a histamine antagonist, an interleukin-1 antagonist and/or a side-effects of certain products, and in particular of certain commetic, dermatological or pharmaceutical active agents.

IT 34031-32-8 Auranofin (pharmaceutical and cosmetic composition and alpha.-tumor necrosis factor antagonists)
```

L4 ANSWER 3 OF 4 USPATFULL ACCESSION NUMBER: 97:73: TITLE: Histar ATFULL
97:73298 USPATFULL
Histamine antagonist, an interleukin-1 antagonist
and/or a TNF alpha antagonist in a cosmetic,
phareaceutical or dermatological composition and
composition obtained
be Lachartiere, Olivier, Paris, France
Breton, Lionel, Versailles, France
Cohen, Catherine, Paris, France
L'Oreal, Paris, France (non-U.S. corporation) INVENTOR(S): PATENT ASSIGNEE(S): NUMBER DATE US 5658581 19970819 US 1995-580291 19951228 (8) PATENT INFORMATION: APPLICATION INFO.: NUMBER DATE FR 1994-15796 19941228 Utility Venkat, Jyothsna Burns, Doane, Swecker & Mathis, L.L.P. PRIORITY INFORMATION: DOCUMENT TYPE: PRIMARY EXAMINER: LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1,8 666 LINE COUNT: 000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF alpha anlagonist in a pharmaceutical or dermatological composition for treating sensitive skins. It relates especially to the use of a histamine antagonist, interleukin-1 antagonist and/or a TNF alpha antagonist for preventing and/or combating skin irritations and/or sores and/or erythema and/nr dysaesthetic sensations and/or sensations of inflammation and/or pruritus and/or prickling and/or tingling and/or discomfort and/or tightness of the skin and/or mucosae. It also relates to a containing a histamine antagonist, an interleukin-1 anlagonist and/or a a TNF alpha antagonist which limits or eliminates the irritant side-effects of certain products, and in particular of certain cosmetic,
dermatological or pharmaceutical active agents.

IT 34031-32-8, Auranofin
(pharmaceutical and cosmetic compns. contg. histamine and interleukin rleukin and .alpha.-tumor necrosis factor antagonists) 34031-32-8 USPATFULL Gold, [1-(thio-kappa.5)-.beta.-D-glucopyranose 2,3,4,6-tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 4 USPATFULL (Continued)

L4 ANSWER 4 OF 4 USPATFULL (Continued)

L4 ANSWER 4 OF 4 USPATFULL
ACCESSION NUMBER: 96:53294 USPATFULL
TITLE: TOPICALLY applied gold organic complex
INVENTOR(S): Papandrea, Ralph A., Collarcy, Australia
Top Gold Pty Limited, Collarcy, Australia (non-U.S. corporation) NUMBER DATE PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.: 15 US 5527779 19960618 US 1994-215409 19940318 (8) Continuation of Ser. No. US 1991-576385, filed on Aug 1991, now abandoned NUMBER DATE NUMBER DATE

AU 1988-7387 19880323
AU 1988-7480 19880328
AU 1989-978 19880318
AU 1989-2313 19890118
Utility
Robinson, Douglas W.
White, Everett
Nikaido Marmelstein Murray & Oram
28 PRIORITY INFORMATION: AU 1988-99/8
AU 1989-2313 19890118
Utility
PRIMARY EXAMINER:
LEGAL REPRESENTATIVE:
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
LINE COUNT: 496
AB It has been surprissingly found that gold compounds may be applied in topical preparations as an effective treatment of local or systemic inflammatory conditions and/or as antibacterial agents. The present invention therefore relates to new pharmaceutical compositions containing gold for topical application, and the use of the composition in treating inflammation and/or as bracterial infection.

IT 34031-32-9, Auranofin (ointments, formulation of, as bactericides and inflammation inhibitors)
RN 34031-32-8 USPATFULL
CN Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetracetato] (triethylphosphine) - (9CI) (CA INDEX NAME)

=>

=> d ibib ab hitstr 1-14

L8 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2000 ACS

(Continued)

```
L8 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:534811 CAPLUS
Implantable medical device with enhanced
biocompatibility and biostability
Fernandes, Brian C. A.; Donovan, Haura G.; Sparer,
Randall V., Casas-Bejar, Jesus W.; Torrianni,
FATENT ASSIGNEE(S): Medtronic Inc., USA
EUR. Pat. Appl., 53 pp.
CODEN: EFEXTOW
DOCUMENT TYPE: Patent
ANGUAGE: Patent
FAMILY ACC. NUM. COUNT: 1

PATENT NO. KIND DATE APPLICATION NO. DATE
FRIENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
FROM THE PROMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
FROM THE PROMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
FROM THE PROMATION:

IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO:
US 1999-117837 19990129

AB An implantable medical device comprising a drug-loaded polymer overlaid
with a fabric that promotes tissue ingrowth is useful in a wide
variety of
tissue engineering applications. The invention includes, for example, prosthetic heart valves, annuloplasty rings, and grafts, having
enhanced
biocompatibility and biostability. Hethods of making and using the implantable medical devices of the invention are also included. An example was give showing in vitro modulation of macrophage phenotype

on dexamethasone-loaded polymer (Pellethane 80A) and its effect on polymer stability in a human macrophage/Fe/stress system.

TRI. DEV (Device component use); TNU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(implantable medical device with enhanced biocompatibility and biostability);

RN 34031-32-8 CAPLUS
CN Gold, [1-(thio-.kappa.s)-.beta.-D-glucopyranose 2, 3, 4, 6-
tetraacetato] (triethylphosphine) - (9CI) (CA INDEX NAME)
```

```
L8 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1999:279689 CAPLUS DOCUMENT NUMBER: 130:316634
 DOCUMENT NUMBER:
TITLE:
                                                      Intraarticular preparation for treatment of
                                                      arthropathy
Suzuki, Makoto: Ishigaki, Kenji: Okada, Minoru:
INVENTOR(S):
                                                     Kenji, Kasai, Shuichi, Imamori, Katsumi
SSP Co., Ltd., Japan
Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
Patent
PATENT ASSIGNEE(S):
DOCUMENT TYPE:
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
          PATENT NO. KIND DATE APPLICATION NO. DATE

EP 911025 A1 19990428 EP 1998-119414 19981014
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
JP 11222425 A2 19990817 JP 1998-293385 19981015
CN 1215589 A 19990505 CN 1998-124109 19981027
RTY APPLN. INFO: JP 1997-294009 19971027
This invention relates to an intra-articular prepn. for the treatment
           arthropathy, which comprises microcapsules of (a) a high-mol.
           cance,
which has biodegradability and biocompatibility, and (b) a drug. When
applied directly to a joint area, this prepn. can achieve a high drug
concn. at the target area, can inhibit occurrence of general side
effect, and can maintain drug efficacy over a long term. The prepn. can
          alleviate the burden on the patient. Microcapsules were prepd. from lactic acid-glycolic acid copolymer 4.5, beclomethasone propionate
         and other ingredients, and their particle sizes and pharmacokinetic parameters were tested.

34031-32-8, Auranofin
RL: TRU (Therapeutic use); BIOL (Biological study); USES (Uses) (intraacticular prepns. for treatment of arthropathy contg. microcapsules of high-mol. substances and pharmaceutically active agents)

34031-32-8 CAPLUS
Gold, (I-(thio-.Kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)
Et3P-Au+S
                                         CH2-OAC
```

```
L8 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued)
REFERENCE COUNT:
                                               (1) Boehringer Ingelheim Kg; EP 0400522 A2 1990
REFERENCE(S):
CAPLUS
                                              (2) Brodack, J; US 5320824 A 1994 CAPIUS
(3) DBY, D; US 5403573 A 1995 CAPIUS
(5) Jernberg, G; WO 91/17744 A1 1991 CAPIUS
(8) Takeda Chemical Industries, Ltd; EP 0442671 A2
1991 CAPIUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
ANSWER 3 OF 14 CAPLUS COPYRIGHT 2000 ACS
SSION NUMBER: 1998:789026 CAPLUS
MENT NUMBER: 130:20568
  DOCUMENT NUMBER:
TITLE:
                                                                                        Treating asthma by preventing and/or
   accommodating for
                                                                                       S-nitrosothiol breakdown
Gaston, Benjamin: Stamler, Jonathan S.: Griffith,
  INVENTOR(S):
  PATENT ASSIGNEE(S):
                                                                                       Duke University, USA; The Medical College of
                                                                                       Research Foundation, Inc.; University of Virginia
                                                                                        Patent Foundation
 SOURCE:
                                                                                       PCT Int. Appl., 32 pp.
CODEN: PIXXD2
 DOCUMENT TYPE:
                                                                                        Patent
 PAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                  PATENT NO.
                                                                           KIND DATE
                                                                                                                                                   APPLICATION NO. DATE
                  PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9852580 A1 19981126 WO 1998-US8978 19980507

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
PT, SE
AU 9872801
PRIORITY APPLN. INFO.:
                                                                                                                                                   AU 1998-72801
US 1997-47336
US 1998-81740
US 1998-81470
WO 1998-US8978
                                                                              A1 19981211
                                                                                                                                                                                                                19980507
                                                                                                                                                                                                                 19980415
                                                                                                                                                                                                               19980507
AB Asthma is ameliorated and mild or moderate asthma is prevented from progressing to more severe asthma by administering agents which
prevent
                  and/or accommodate for S-nitrosothiol breakdown, e.g. inhibitors of .gamma.-glutamyl transpeptidase or xanthine oxidase, chelators of
coppe
                  and/or heme or non-heme iron, and NO donors. Thus, administration of
                 mM soln. of bathocuproine disulfonate via inhalation as an aerosol at
                 dose of 0.01 mL/kg improve symptoms in a 24-yr old woman with severe asthma with symptoms of dyspnea on exertion, cough, and prolonged expiration. The method reduces requirements for systemic corticosteroids for the treatment of severe asthma.
                corticosteroids for the treatment of the control of
                                                         CAPLUS
                 34031-32-8 CAPLUS Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-
```

LB ANSWER 4 OF 14 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:426206 CAPLUS
DOCUMENT NUMBER: 1998:426206 CAPLUS
DOCUMENT NUMBER: 1998:426206 CAPLUS
COCOMENT NUMBER: 1098:426206 CAPLUS
BERNSTEIN, 129:169393
AUTHOR(S): Bernstein, 1 Leonard; Bernstein, David I.;
Bernstein, Jonathan A.
CORPORATE SOURCE: University of Cincinnati Medical Center,
Cincinnati, OH, USA
SOURCE: BibOrups (1997), 8(3), 205-215
CODEN: BIDER4; ISSN: 1173-8804
Adis International Ltd.
JOURNENT TYPE: JOURNAL General Review
LANGUAGE: Brights A Leonard; General Review
LANGUAGE: A subset of corticosteroid-dependent
patients require substantial amts. of daily systemic
coorticosteroids, a subset of corticosteroid-dependent
patients require substantial amts. of daily systemic
coorticosteroids for adequate control. Several anti-inflammatory
modulating agents (auranofin, methotrexate and cyclosporin) have been
evaluated for their corticosteroid-sparing properties under such
circumstances. This anal was gleaned primarily from randomized,
double-blind, placebo-controlled trials of these agents. Global
assessment of corticosteroid-sparing efficacy of these drugs
revealed an advantage of auranofin over both methotrexate and
cyclosporin.
In addn., the comparative adverse event profiles of these drugs
indicated
that auranofin exhibited milder, nore tolerable adverse effects.
Therefore, auranofin presents a better risk: benefit option in initial
attempts to wean dependent patients from corticosteroids.
IT 34031-32-8, Auranofin
RL: ADV (Adverse effect, including toxicity); BAC (Biological
study); USES (Uses)
(auranofin vs. methotrexate and cyclosporin as a corticosteroid
-sparing agent in humans with severe asthma)

N 34031-32-9 a CAPLUS
CN Gold, [1-(thio-.kappa.S)-.beta.-D-glucopycanose 2, 3, 4, 6tetracetato] (triethylphosphine) - (9CI) (CA INDEX NAME)

```
Et3P-Au±S-0 CH2-OAC
```

ANSWER 3 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) tetraacetato](triethylphosphine) - (9CI) (CA INDEX NAME)

REFERENCE COUNT: REFERENCE(S):

(1) Stamler, US 5380758 A 1995 CAPLUS (2) Stamler, US 5574068 A 1996

INVENTOR(S):

INVENTOR(S):

INVENTOR(S):

PATENT ASSIGNEE(S):

Medical Innovations Ltd., Australia; Thomas, Richard Edward

SOURCE:

PCT Int. Appl., 34 pp.

CODEN: PIXXD2

PATENT INFORMATION:

PATENT NO. KIND DATE

APPLICATION NO. DATE

PATENT INFORMATION:

PATENT NO. KIND DATE

APPLICATION NO. DATE

APPLICATION NO. DATE

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JF, KE, KG, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, MD, HG, MX, MN, MW, MX, NO, NZ,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TH, TR, TT, UA, UG,

US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TH,

RW: GH, KE, LS, MW, SD, S2, UG, ZW, AT, BE, CH, DE, DK, ES, FI,

GA, GN, HL, MR, NE, SN, TD, TG

AU 9747671 Al 19990519

AU 9747671 Al 19990529

AU 1997-47671 19971104

R: AT, EE, CH, DE, DK, ES, FR, GB, GR, IT, LI, PT, IE

CN 1235550 A 1999110 EP 1997-910157 19971104

AB This invention relates to a method of treating an immune-mediated disorder

having one or more manifestations. The method comprises administering to

a patient requiring such treatment a gold compd. and at least one corticosteroid, wherein the at least one corticosteroid verticosteroid, wherein the at least one corticosteroid verticosteroid verticosteroid such towards one of the manifestations of said disorder. The invention also relates to a pharmaceutical compn. suitable for use in the method. The synergistic effect of auranofin with various corticosteroid was demonstrated with betamethesone diproprionate, flueucinolome accorticosteroid such disorder or to exhibit equal action towards each manifestation of said disorder. The invention also relates to a pharmaceutical compn. suitable for use in the method. The synergistic effect of auranofin with various corticosteroids was demonstrated with betamethesone diproprionate, flueucinolome accorticoste

L8 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:323140 CAPLUS
DOCUMENT NUMBER: 129:19685
TITLE: Synergistic gold and 60

ANSWER 5 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued)

ANSYER 5 OF 14 CAPLUS COLLEGE.

14031-32-8, Autranofin

14031-32-8, Autranofin

14031-32-8, Discount of fector, except adverse); THU

(Therapautic use); BIOL (Biological study); USES (Uses)

(synergistic gold and coeticosteroid-contg. compns.)

34031-32-8 CAPLUS

Gold, (1-(thio-.kapps.S)-.beta.-D-glucopyranose; 2,3,4,6-tetraacetato)(triethylphosphine)- (9CI) (CA INDEX NAME)

ANSWER 6 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given

g
starch, polyethylene, glycerol monostearate, and vegetable oil.
34031-32-8, Auranofin
RL: PEP (Physical, engineering or chemical process): THU (Therapeutic
use): BIOL (Biological study): PROC (Process): USES (Uses)
(embedding and encapsulation of controlled release particles)
34031-32-8 CAPUS
Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

L8 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:293427 CAPLUS
DOCUMENT NUMBER: 129:8557
TITLE: 129:8597
Embedding and encapsulation of controlled release particles
Van Lengerich, Bernhard H.
Van Lengerich, Bernhard H., USA
PCT Int. Appl., 63 pp.
CODEN: PIXXD2
Patent INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE: DOCUMENT TYPE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9818610 A1 199980507 WO 1997-US18984 19971027
W: AU, CA, JP, NO, PL, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, SE AU 9749915 Al 19980522 AU 1997-49915 19971027 EP 935523 Al 19990818 EP 1997-912825 19971027 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, 1E, FI NO 9902036 A 19990428 PRIORITY APPLN. INFO.: NO 1999-2036 19990428 PRITY APPLN. INFO.: US 1996-29036 19990428 19961028 US 1997-52717 19970716 US 1997-52717 19970716 WO 1997-US18984 19971027 Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or lity oxidizable pharmaceutically, biol., or nutritionally active component are

continuously produced without substantial destruction of the matrix
material or encapsulant. A release-rate controlling component is
incorporated into the matrix to control the rate of release of the
encapsulant from the particles. The addnl. component may be a
hydrophobic opmonic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions plasticize the plasticizable material without substantially plasticize the plasticizable material and to obtain a substantially obspaceous plasticized mass. The plasticizer content is substantially reduced and the temp, of the plasticized mass is substantially reduced. substantially reduced and the temp. of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixt. The mixt. is extruded though a die without substantial

L8 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1998:87949 CAPLUS DOCUMENT NUMBER: 128:123562

DOCUMENT NUMBER:

TITLE: A simple inflammation model that distinguishes between

the actions of anti-inflammatory and anti-rheumatic

AUTHOR(S):

Lewis, E. J.; Bishop, J.; Aspinall, S. J. Roche Discovery Welwyn, Welwyn Garden City, AL7 CORPORATE SOURCE:

3AY.

SOURCE: Inflammation Res. (1998), 47(1), 26-35 CODEN: INREFB: ISSN: 1023-3830

PUBLISHER: Birkhaeuser Verlag

DOCUMENT TYPE:

LANGUAGE:

MAGE: Souther
MAGE: English
The effects of anti-inflammatory and anti-rheumatic drugs on paw

avelling and changes in plasma levels of acute phase proteins (AFPs) during

sinflammation in the rat was investigated. Inflammation was induced in rats by the injection of adjuvant and the animals were bled five days later and plasma levels of seromucoid, haptoglobin, ceruloplasmin and albumin were detd. spectrophotometrically using a Cobas-bio

analyzer. The effects of daily administration of a variety of drugs

to treat arthritis were detd. on paw swelling and APP levels.

of the adjuvant induced a pronounced change in APP levels which

correlated

elated with the increase in paw swelling. In general, the NSAIDs tested significantly reduced paw swelling and significantly increased levels

haptoglobin and ceruloplasmin in a dose-related manner. Two

of steroids were administered, the higher dose reduced swelling, and reduced levels of seromucoid, haptoglobin and ceruloplasmin, but

ou albumin levels, the lower dose also reduced paw swelling, but the only change in APPs was increased albumin levels. Anti-theumatic drugs

gold salts reduced levels of some APPs (seromucoid, haptoglobin and ceruloplasmin) without reducing paw swelling. Immunomodulators had a variety of effects on inflammation and APPs depending on mechanism of action. It is concluded that the different classes of anti-inflammatory/anti-rheumatic drug tested show distinct profiles of activity against APPs and paw swelling. These differential effects

result from modulation of cytokine activity.
34031-32-8, Auranofin
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological atudy); USES (Uses)
(a simple inflammation model distinguishes between the actions of anti-inflammatory and anti-rheumatic drugs)
34031-32-8 CAPLUS

L9 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued)
CN Gold, [1-(thio-.kappa.5)-.beta.-D-glucopyranose 2,3,4,6tatraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

L8 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued)

L8 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1997:684253 CAPLUS DOCUMENT NUMBER: 127:336649 TITLE: Process for encapsulation of caplets in a capsule solid dosage forms obtainable by this process Cade, Dominique, Maes, Paul, Scott, Robert Warner-Lambert Co., USA PCT Int. Appl., 24 pp. CODEM: PIXXIO2 Patent INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: English PATENT NO. PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9737629 A1 19971016 WO 1997-US4482 19970324
W: AL, CA, CN, JP, XR, LT, LV, MX, NO, RO, S1
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, KIND DATE APPLICATION NO. DATE SE CA 2250017 AA 19971016 CA 1997-2250017 19970324 EP 891180 A1 19990120 EP 1997-916858 19970324 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE, FI
CN 1215322 A 19990428
JP 2000508552 T2 20000711
PRIORITY APPLN. INFO.: CN 1997-193572 19970324 JP 1997-536220 19970324 US 1996-628823 19960405 WO 1997-US4482 19970324 A process for encapsulation of caplets in a capsule comprises the following steps: (a) providing empty capsule parts: (b) filling at one of the capsule parts with one or more caplets; (c) putting the ne parts together, and (d) treating the combined parts by cold shrinking. The solid dosage forms obtainable by such a process are tamper-proof that they cannot be opened in a way to be reassembled without showing opening process.
34031-32-9, Auranofin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for encapsulation of caplets in capsules)
34031-32-9 CAPLUS
GOLd, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

L8 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1997:520401 CAPLUS DOCUMENT NUMBER: 127:214792 Pharmacological influence of antirheumatic drugs TITLE: proteoglycanases from interleukin-1 treated articular Steinmeyer, Juergen; Daufeldt, Sabine Department of Pharmacology and Toxicology, AUTHOR(S): CORPORATE SOURCE: Rheinische Friedrich-Wilhelms-Universitat Bonn, Friedrich-Wilhelms-Universitat Bonn, Bonn, 53113, SOURCE: PUBLISHER: proteoglycanolytic activities of matrix metalloproteinases (MMPs), det. whether drugs which inhibit these enzymes also modulate the biosynthesis and release of proteoglycams (PGs) from biosynthesis and release of process. In interleukin-1-(IL-1) treated articular cartilage explants. The cartilage-bone marrow ext. the glycosaminoglycan-peptide complex (DAK-16) dose-dependently inhibited MMP proteoglycanases in vitro when tested at concns. ranging from 0.555 mg/mL, displaying an IC50 value of 31.78 mg/mL and 10.64 mg/mL (1.9 times. 10-4 H) resp.

(R,S)-N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl-L-phenylalaninamide (U-24522) proved to be a potent inhibitor of MMP proteoglycanases (IC50 value 1.8 .times. 10-9 M). of the other tested drugs, such as possible chondroprotective drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), disease modifying antirheumatic drugs (DMARDs), glucocorticoids and harming-operation anctivements study (MMANUS), glucocottectes and angiotensin-converting enzyme inhibitors tested at a concn. of 10-4 M displayed any significant inhibition. Only U-24522, tested at a concn. ranging from 10-4 to 10-6 $\rm M_{\odot}$ M, significantly inhibited the IL-1-induced augmentation of PG loss from cartilage explants into the nutrient media, whereas DAK-16 and the cartilage-bone marrow ext. were ineffective. DAK-16 and the cartilage-bone marrow ext. did not modulate the IL-1-mediated reduced biosynthesis and aggregability of PGs by the cartilage explants. The addn of 10-5 M U-24522, however, partially maintained the agability aggregability
of PGs ex vivo. In our expts., both possible chondroprotective drugs

well as U-24522 demonstrated no cytotoxic effects on chondrocytes.

ANSWER 9 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) 34031-32-8, Auranofin RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); TMU (Therapeutic use); BIOL (Biological study); USES (Uses) (effects of antirheumatic drugs on proteoglycanases from interleukin-1 treated articular cartilage)
34031-32-8 CAPLUS Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

ANSWER 10 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) 34031-32-8, Auranofin RL: BAC (Biological activity or effector, except adverse); THU (Therapoutic use); BIOL (Biological study); USES (Uses) (auranofin effect on COX-1- and COX-2-dependent PGE2 prodm. in tion
to mechanism of antirheumatic and antiinflammatory activities)
34031-32-8 CAPIUS
601d, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6tetraacetato)(triethylphosphine)- (9CI) (CA INDEX NAME)

L8 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1997:318911 CAPLUS DOCUMENT NUMBER: 127:13186 Prostoclassic Prostaglandin E2 production dependent upon cycloxygenase-1 and cycloxygenase-2 and its contradictory modulation by auranofin in rat peritoneal macrophages Yamada, Masateru, Niki, Hisae, Yamashita, AUTHOR(S): Masamichi; Mue, Suetsugu: Chuchi, Kazuo Department Pathophysiological Biochemistry, CORPORATE SOURCE: Faculty Pharmaceutical Sciences, Tohoku University. Japan J. Pharmacol. Exp. Ther. (1997), 281(2), 1005-1012 CODEN: JPETAB, ISSN: 0022-3565 Williams & Wilkins CODEN: JPETABJ ISSN: 0022-3565

PUBLISHER: Williams 4 Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat peritoneal macrophages were incubated in the presence of
cycloheximide
or dexamathasone to inhibit the induction of cyclooxygenase
(COX)-2 protein synthesis. Thereafter, when the macrophages were
incubated in the presence of arachidonic acid, PGE2 prodn. was incubated in the presence of arachidonic acid, PGEZ prodn. was increased.

Western blot anal. demonstrated that COX-2 protein levels were low and were not affected by arachidonic acid treatment. COX-1 protein levels were not affected by arachidonic acid treatment either. The COX-2 inhibitors NS-398 and nimesulide only slightly inhibited PGEZ prodn., whereas the COX-1/COX-2 inhibitors indomethacin, piroxicam and tenoxicam strongly inhibited PGEZ prodn. This suggests that under these conditions,

PGEZ prodn. is dependent on COX-1. After the macrophages were treated with aspirin to inactivate existing COX-1 and COX-2, however, treatment with aspirin to inactivate existing COX-1 and COX-2, however, treatment with 12-0-tetradecanoylphorbol 13-acetate increased PGE2 prodn. Furthermore, COX-2 protein levels were markedly increased by 12-0-tetradecanoylphorbol 13-acetate treatment, whereas COX-1 protein levels did not change. In this case, both the COX-2 and the COX-1/COX-2 inhibitors inhibited PGE2 prodn. This suggests that under these conditions, PGE2 prodn. is dependent on COX-2. Effects of auranofin COX-1-dependent and COX-2-dependent PGE2 prodn. were examd. We found auranofin stimulated COX-1-dependent PGE2 prodn. but inhibited COX-2-dependent PGE2 prodn. in a concn.-dependent manner. The latter effect was found to be due to the inhibition of COX-2 protein ction.

These findings might explain the mechanism of the antirheumatic and anti-inflammatory activities of auranofin.

L8 ANSWER 11 OF 14 CAPLUS COFYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:587923 CAPLUS
DOCUMENT NUMBER: 125:265598
TITLE: auranofin in A placebo-controlled multicenter study of the treatment of patients with corticosteroid -dependent asthma Bernstein, I. Leonard; Bernstein, David I.; Dubb, Jeffrey W.; Faiferman, Isidore; Wallin, Bruce; Bronsky, Edwin; Spector, Sheldon L.; Nathan, AUTHOR (S): Robert A.; Nelson, Harold S.; et al. College Medicine, University Cincinnati, CORPORATE SOURCE: Cincinnati, OH, 45267, USA J. Allergy Clin. Immunol. (1996), 98(2), 317-324 CODEN: JACIBY; ISSN: 0091-6749 SOURCE: DOCUMENT TYPE: LANGUAGE: Journal English Previous clin. studies have demonstrated that injectable gold salts the oral gold compd., auranofin, possess significant steroid-sparing effects in the treatment of asthma. Objectives: The objectives of investigation were to det. whether auranofin could reduce oral corticosteroid requirements and to evaluate the safety of auranofin in the treatment of chronic corticosteroid-dependent asthma. Methods: Patients with asthma were eligible if they required least 10 mg of prednisone per day for control and prevention of asthma exacerbations. Two hundred seventy-nine patients with chronic corticosteroid-dependent asthma (requiring .gtoreq. 10 mg/day) were randomized to receive auranofin, 3 mg twice daily, or placebo

an 8-mo clin. trial, which was divided into three phases including: a baseline period (phase I), a 6-mo double-blind treatment and steroid

period (phase II), and a 4-wk posttreatment observation period during which steroid and auranofin doses or placebo doses were maintained at levels achieved by the end of phase II (phase III). The primary

efficacy
variable was "therapeutic success" or redn. of daily
continosteroid use by 50% or more. Results: The proportion of
patients in the auranofin group achieving therapeutic success (41%)

significantly higher than that in the placebo group (27%) (p = 0.01). This effect was greatest in patients requiring 10 to 19 mg of oral prednisone per day at baseline (p < 0.001). In all treated patients, including those who did and did not complete the trial, significant

(.gtoreq.50% of baseline) in oral corticosteroid dowage was achieved in the auranofin group (60%) compared with the placebo group (32%) (pc 0.00%). There were no significant differences between treatment groups in symptoms, concomitant medication use, or lung function. Mean serum total [gR levels decreased significantly from baseline in the auranofin group (-44.63 IU/mL) compared with the

L0 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) group (p = 0.001). Gastrointestinal and cutaneous adverse events were greater in the auranofin group. Conclusions: Auranofin demonstrated a steroid-sparing effect without concomitant worsening of symptoms or lung function and appeared to be more effective in patients dependent on 10 to 19 mg of prednisone per day. Therefore this study has demonstrated that auranofin is useful as a steroid-sparing agent in the treatment of chronic corticosteroid-dependent asthma.

17 34031-32-8, Auranofin RI: BAC (Biological activity or effector, except adverse); TNU (Therapeutic use); BIOL (Biological'study); USES (Uses) (placebo-controlled multicenter study of auranofin in the treatment of humans with corticosteroid-dependent asthma)

RN 34031-32-8 (ARUS)

CN Gold, [1-(thio-kappa.S)-beta.-D-qlucopyranose 2,3,4,6-tetraacetato] (triethylphosphine) - (9CI) (CA INDEX NAME)

L8 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued)

L8 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1996:464557 CAPLUS DOCUMENT NUMBER: 125:96163 TITLE: Process for encapsulation of caplets in a capsule solid dosage forms obtainable by such process Amey, James: Cade, Dominique: Maes, Paul; Scott, Robert Warner-Lambert Company, USA PCT Int. Appl., 23 pp. CODEN: PIXXU2 INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: Patent English PATENT NO. KIND DATE APPLICATION NO. DATE PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9618370 A1 19960620 WO 1995-US14651 19951109
W: CA, CN, JP, KR, MX
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 797424 B1 20000712
EP 1997424 B1 20000712 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE

CN 1170346

JP 11500326

AT 194486

US 6080426

CA 2214923

PRIORITY APPLN. INFO.: CN 1995-196811 19951109
JP 1995-518819 19951109
AT 1995-939890 19951109
US 1996-685549 19960111
CA 1997-2214923 19970909
US 1994-356137 19941216
WO 1995-US14651 19951109 A T2 E 19980114 19990112 20000715 20000627 19990309 A AA A process for encapsulation of caplets in a capsule comprises the following steps: (a) providing empty capsule parts: (b) filling at one of the capsule parts with one or more caplets; (c) putting the capsule use
parts together, and (d) treating the combined parts by cold shrinking.
The solid dosage forms obtainable by such a process are tamper-proof that they cannot be opened in a way to be reassembled without showing opening process.
34031-32-8, Auranofin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of caplets in capsules in tamper-proof forms)
34031-32-8 CAPLUS
Gold, [1-(thio-kappa.S)-.beta.-D-glucopyranose 2,3,4,6tetraacetato)(triethylphosphine) - (9CI) (CA INDEX NAME)

L8 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1996:375709 CAPLUS DOCUMENT NUMBER: 125:48726 DOCUMENT NUMBER: TITLE: Type II collagen-induced arthritis in the diabetic-resistant BioBreeding rat: inflammatory and histopathological features of joint pathology and effects of antiinflammatory and antirheumatic drugs on this chronic arthritic process Smith, Robert J., Sly, Laurel M. Dep. Cell Biol. Inflammation Res., Pharmacia & AUTHOR(S): CORPORATE SOURCE: Upjohn, hh, Inc., Kalamazoo, MI, USA
CE: J. Pharmacol. Exp. Ther. (1996), 277(3), 1801-1813
CODEN: JPETAB, ISSN: 0022-3565
MENT TYPE: Journal
DUAGE: English
Diabetic-resistant (DR) BioBreeding (BB) rats developed an erosive SOURCE: DOCUMENT TYPE: hind paw arthritis when immunized with an emulsion of bovine type II collagen
(CII) and incomplete Freund's adjuvant. Macroscopic clin. evidence of
type II collagen-induced arthritis (CIA) first appeared as periarticular reticular erythema and edema in the hind paws between days 9 and 10 post-immunization with CII. The incidence of CIA was 100% by day 11 the CII-challenged rats; and CIA severity progressed over a 28-day with radiog. evaluation revealing focal resorption of bone together osteophyte formation in the tibiotarsal joint and soft tissue swelling; the histopathol. of CIA included an hyperplastic synovium that eed and eroded articular cartilage at the joint margins, and subchondral bone resorption assood. with bone-derived, multinucleated cell-contg, granulomatous lesions in the rat hind paw. The corticosteroid, methylprednisolone (medrol), and the nonsteroidal antiinflammatory flurbiprofen (Ansaid), administered at 2 mg/kg (p.o.), suppressed the clin. signs of CIA, and caused 79 to 83% inhibition of hind paw inflammation. However, methylprednisolone, but not flurbiprofen, inhibited the joint pathol. in CIA. The antirheumatic drugs, cyclophosphamide (cytoxan, 5 mg/kg, p.o.) and cycloportin A (CBA, 25 mg/kg, p.o.) suppressed the cartilage erosion in inflamed rat joints, exerted marked inhibition (89-100%) of hind paw swelling. (0.15 mg/kg, p.o.) treatment reduced hind paw swelling (48%), whereas azathioprine, D-penicillamine (DP) and the oral gold prepn., arranting are the pentitial and (b) and the oral gold preph.,
were inactive. Anti-CII antibody titers were completely suppressed by
cyclosporin A and cytoxan. Radiog. evidence of protection from bone
resorption, osteophyte formation and soft tissue swelling was
apparent in

ANSWER 13 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) the tibiotarsal joints of cytoxan, cyclosporin A, methylprednisolone

methotrexate-treated rat.
34031-32-8, Auranofin
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(type II collagen-induced arthritis in the diabetic-resistant
BioBreeding rat: histopathol. features of joint pathol. and BioBreeding ret. NATION CONTROL OF STREET CONTROL OF STREET CAPTUS

RN 34031-32-8 CAPTUS

CN Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetaacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

ANSWER 14 OF 14 CAPLUS COPYRIGHT 2000 ACS (Continued) testing agents, including those of limited or unknown systemic bioavailability, in order to discover novel therapeutic agents for preventing collagen degrdn. in connective tissue diseases such as

arthritis. 34031-32-8, Auranofin

RI: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (collagen-gelled cotton buds model of collagen degran. and collagenase

agenase inhibitors and other agents effects) 34031-32-8 CAPUUS Gold, [1-(thio-.kappa.S)-.beta.-D-glucopyranose 2,3,4,6-tetraacetato](triethylphosphine)- (9CI) (CA INDEX NAME)

L8 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1995:436892 CAPLUS DOCUMENT NUMBER: 122:255792

A simple in vivo model of collagen degradation

collagen-gelled cotton buds: the effects of collagenase inhibitors and other agents Karran, Eric H.; Dodgson, Kathryn; Harris, Sonia AUTHOR (S):

Markwell, Roger E.; Harper, Gregory P. SmithKline Beecham Pharmaceuticals, Essex, CM19

CORPORATE SOURCE:

Inflammation Res. (1995), 44(1), 36-46 CODEN: INREFB; ISSN: 1023-3830

COURN: INKERD; 135H. 1425 555
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple in vivo model of collagen degrdh. has been developed, and the
effects of various agents have been tested. Type I collagen was

prepd.
from rat skin and acetylated with either [3H] - or [14C] acetic

from rat skin and acetylated with either [3Hj or [14U] acetic anhydride.

The radiolabeled collagen was added to sterile cotton buds and incubated at 37 degree.C to allow the collagen to form native fibrile that were firmly adsorbed to the cotton matrix. After a.c. implantation of the collagen-gelled cotton buds into rats, the radiolabeled collagen was progressively removed over a period of weeks by an infiltrating granuloma.

Of the agents that were administered directly into the cotton buds using

g s.c. implanted osmotic mini-pumps, only the synthetic collagenase inhibitors CI-A (contg. a hydroxamate moiety as a zinc ligand) and

(contg. a thiol moiety as a zinc ligand) were able to prevent the removal

val
of collagen: their efficacy correlated with the level of collagenase
inhibitory activity assayed in the exudate fluid sequestered within

cotton bud granuloma. Of the agents that were administered

systemically, including anti-inflammatory drugs and other compds. used as therapies

arthritis, only hydrocortisone was able to inhibit the removal of radiolabeled collagen. These results suggest that, in this model, interstitial collagenase, a member of the matrix metalloproteinase

family,
comprised the major degradative pathway for collagen. The

=> d his

	(FILE 'HOME' ENTERED AT 10:24:37 ON 23 AUG 2000)
L1	FILE 'REGISTRY' ENTERED AT 10:24:41 ON 23 AUG 2000 1 SS AURANOFIN/CN
L2 L3 L4 M	FILE 'USPATFULL' ENTERED AT 10:24:54 ON 23 AUG 2000 20 S L1 0 S L2 (P)CORTICOSTEROID? 4 S L2 AND (HYDROCORTISONE OR BETAMETHASONE OR DEXAMETHASONE OR
L5 L6 M L7 L8	FILE 'CAPLUS' ENTERED AT 10:29:12 ON 23 AUG 2000 80 S L1/THU 10 S L5 AND (HYDROCORTISONE OR BETAMETHASONE OR DEXAMETHASONE OR 5 S L5 AND CORTICOSTEROID? 14 S L6 OR L7